ABSTRACT

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Title of Thesis **Copper chelating potential of iron chelators from the group of aroylhydrazones**

Copper is one of the essential trace elements. It is present in two oxidation-reduction forms Cu+ and Cu2+ in the human body. The ability of an easy transformation between this two forms is the crucial feature for the activity of copper enzymes, like superoxide dismutase and cytochrome c oxidase. Copper kinetics is quite complicated. The key organ which affects copper kinetics is the liver, but the small intestine plays an important regulatory role too.

There are disorders, which are associated with both copper deficiency and accumulation. The best known disorder caused by copper excess is Wilson´s disease. It is caused by a mutation in the ATP7B gene. It codes a transporter, which is responsible for elimination of copper. Excessive accumulation of copper causes several symptoms, mainly hepatic and neurological problems. Wilson´s disease is treated by chelators, which bind the excess of metal ions in the organism.

The aim of my thesis was to verify the copper–chelation efficiency of three selected iron chelators. The chelators were choosen from the group of aroylhydrazones: pyridoxal isonicotinoyl hydrazone (PIH), salicylaldehyde isonicotinoyl hydrazone (SIH) and 2-pyridylcarboxaldehyde-2-thiophenecarboxyl hydrazone (PCTH). Chelation was experimentally tested by two methods in a pH range of 4.5 to 7.5. In the first method, hematoxylin (HEM) was used as an indicator. This was used as an approximate determination. In the second method, disodium salt of bathocuproinedisulfonic acid (BCS) was used. This indicator was more accurate and sensitive.

The most effective chelators were PIH and SIH. These substances formed stable complexes in a pH range of 6.8 – 7.5 with approximate stoichiometry 1:1. There was no significant difference between these substances in chelation efficiency. SIH and PIH were not able to form stable complexes with cuprous ions at pH 4.5 as there was some decrease of chelation. SIH was slightly, but significantly, more effective at pH 4.5 – 5.5 than PIH. PCTH was clearly a weaker chelator in comparison to the two above mentioned. PCTH showed chelation activity with cupric ions at pH 6.-8 – 7.5 with corresponding stoichiometry 3:2, but complexes were unstable. In lower pH conditions, it was necessary to use an excess of this chelator to reach sufficient chelation. These complexes were unstable.

In conclusion, the known iron chelators SIH and PIH form stable complexes with both cupric and cuprous ions in neutral and slightly acidic conditions.